Psoriatic Arthritis in clinical practice

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Clinical case

- Male patient 34 years old ,diabetic with BMI 31 work as banker
- C/O long standing low back pain mainly in late night and early morning with stiffness affect back, hand and feet for about half an hour
- Patient sought medical advice and diagnosed as lumbar spondylosis and advised to frequent change of position , change his seat and prescribed NSAID and muscle relaxant but patient not fully satisfied
- Few months later patient developed right third toe swelling … diagnosed as bacterial infection with antibiotic described but not resolved however he noticed improvement when he use NSAID for his back
- Patient have small psoriatic patches on his hands few years ago and using topical ointment

Does this patient have psoriatic arthritis?

Diagnosis

In the assessment of a patient for possible PsA, it is important to focus on the history and physical examination of the **five key domains of this disease**, which include

- Skin manifestations of psoriasis,
- inflammatory peripheral arthritis,
- spondylitis,
- enthesitis,
- dactylitis.

CASPAR (**Cl**A**S**Sification criteria for **P**soriatic **AR**thritis) Criteria

A patient must have inflammatory articular disease (joint, spine or entheseal) and ≥ 3 points from the following categories

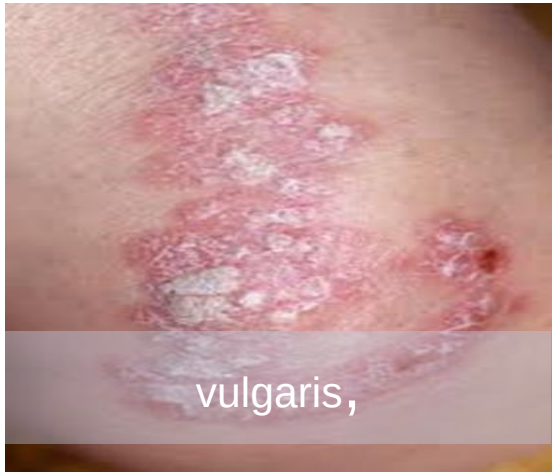
Category	Description	Points
Current psoriasis or personal or family history of psoriasis	Current psoriasis: skin or plaque disease confirmed by rheumatologist or dermatologist. Personal history: obtained from patient, family physician, dermatologist, rheumatologist or other qualified health care provider. Family history: presence of psoriasis in 1° or 2° relative as reported by patient.	2 (current) OR 1 (history)
Psoriatic nail dystrophy on current examination	Onycholysis, pitting, hyperkeratosis.	1
Negative rheumatoid factor (RF)	Any method except latex, but preferably Enzyme-linked immunosorbent assay (ELISA) or nephelometry, using local laboratory reference range.	1
Dactylitis (current or on history as recorded by rheumatologist)	Swelling of an entire digit	1
Radiographic evidence of juxta-articular new-bone formation.	Ill-defined ossification near joint margins but excluding osteophyte formation on plain XRays of the hand or foot.	1

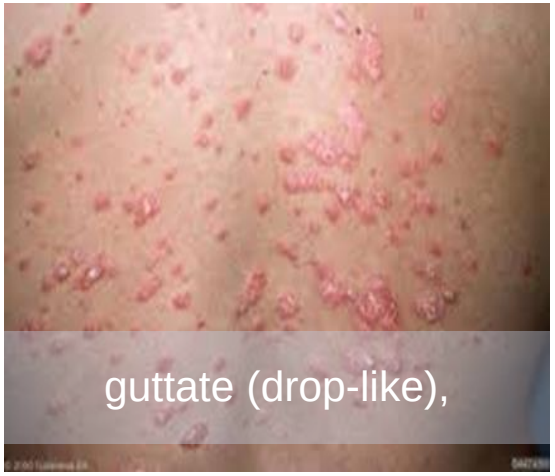
Sensitivity 91.4% Specificity 98.7%

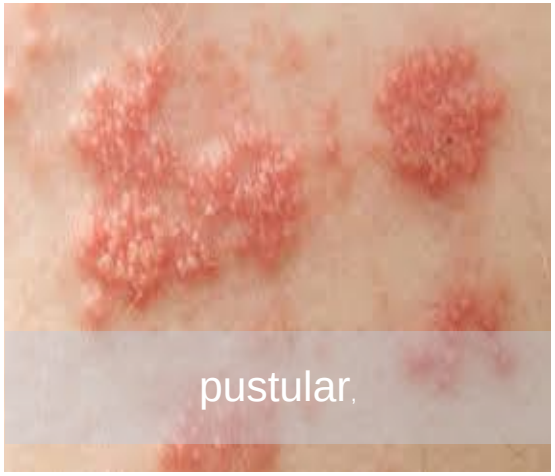
Taylor et al. Classification Criteria for Psoriatic Arthritis: development of new criteria from a large international study. Arth Rheum 2006;54:2665-2673

Psoriasis

Several forms of psoriasis can be associated with arthritis, including







Psoriasis in relation to PsA

The most common form is **psoriasis vulgaris**

on average, the psoriasis precedes the arthritis by **ten years**

in 15% of patients, the skin and joints manifest **concurrently**

in another 15% joint symptoms **precede** the onset of psoriasis.

A small subset with arthritic features (clinical and radiographic) but **no skin** involvement, labeled "**sine psoriasis**," has also been described.

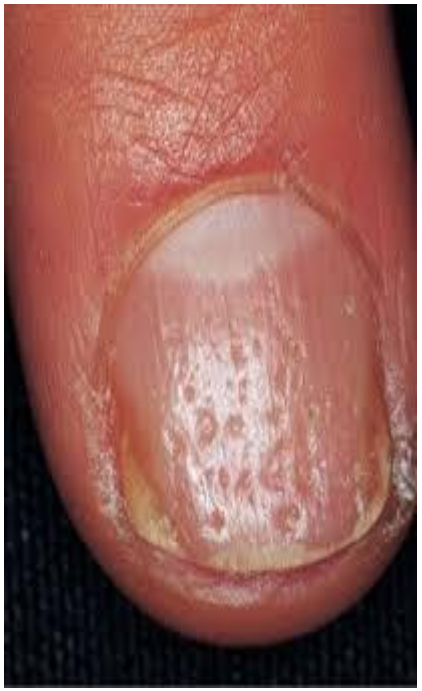
It is estimated that approximately **25% of psoriasis patients develop arthritis.**

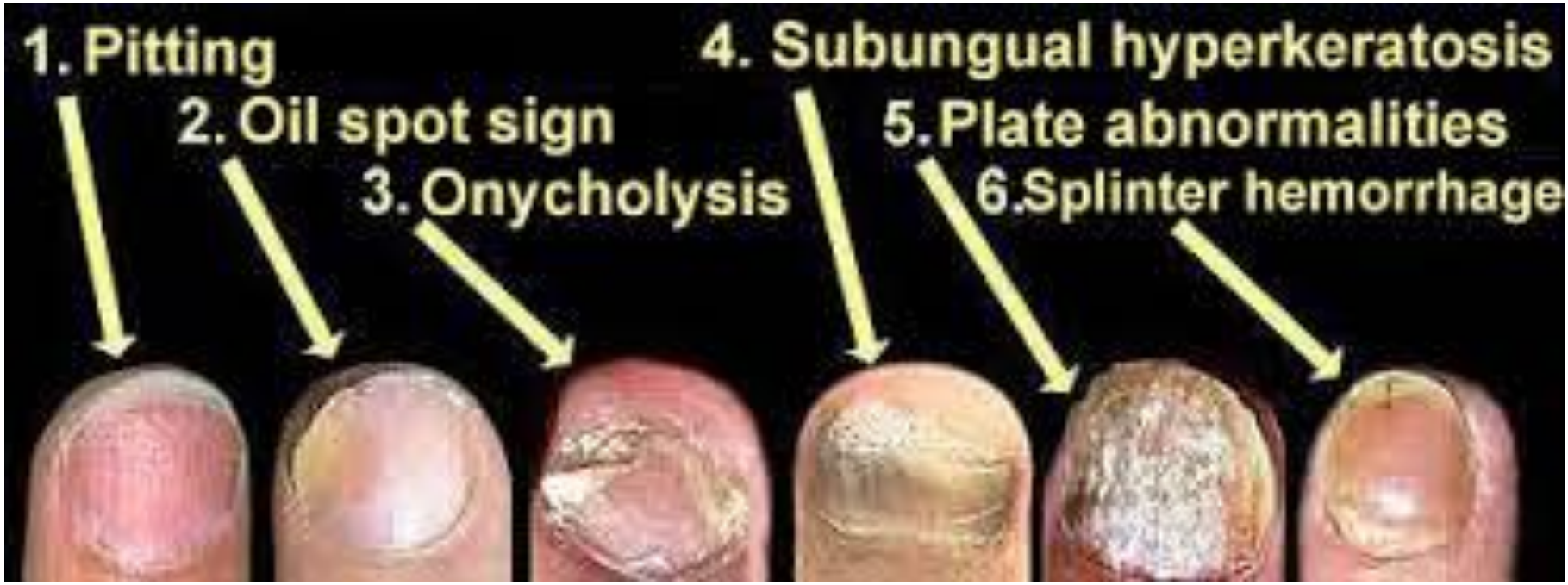
Patients with **more severe psoriasis are more likely to have arthritis,**

the **correlation between severity** of skin and joint disease in an individual patient is **quite low**.

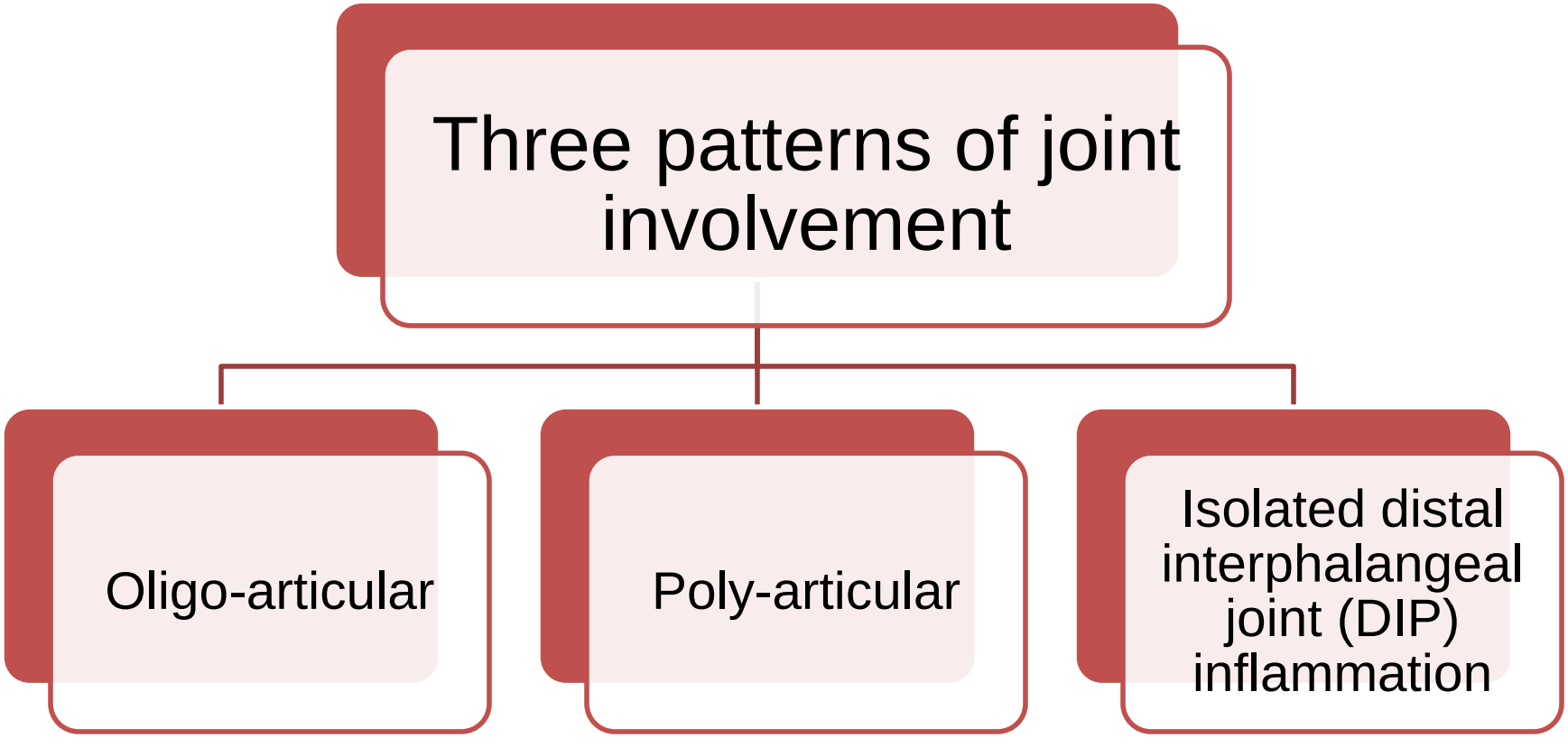
Nail changes

Nail lesions are observed in a high proportion of PsA patients and take on many forms (pits, onycholysis, ridges, and erosions).




1. Pitting
2. Oil spot sign
3. Onycholysis
4. Subungual hyperkeratosis
5. Plate abnormalities
6. Splinter hemorrhage

Peripheral arthritis



Peripheral arthritis

Patients present with

- **joint pain,**
- **stiffness,**
- **redness,**
- **but joints are less tender in comparison to rheumatoid arthritis (RA).**

intense purplish discoloration over the joint could be observed,

distal limb edema has also been reported.

PsA distribution is quite unique in that involvement of individual rays of the hand or feet may differ markedly with juxtaposed (in one digit) or alternating (between digits) areas of excessive bone resorption and new bone formation.

Peripheral arthritis

As a rule, polyarticular disease and erosions are markers for disease progression.

A widely quoted study of an early PsA cohort with peripheral arthritis reported that approximately half the patients manifested erosions after 2 years and the majority were on disease-modifying anti-rheumatic agents (DMARDs) at this time point.

Arthritis mutilans, a rare form of PsA, marked by excessive bone resorption with digits that are telescoped and flail, has been observed much less commonly over the last decade for unknown reasons.

Isolated DIP disease is rare and often associated with marked nail inflammation.

Spondylitis

The prevalence of axial involvement in PsA

- Estimates of **24-50%** in the **lower spine and sacroiliac (SI) joints**
- Estimates of **60%** in **cervical spine** based on radiologic criteria.

Isolated spinal disease

- **Very uncommon in PsA**,
- **Differentiation from axial spondyloarthritis** (ankylosing spondylitis, non-radiographic axial spondyloarthritis) **may not be possible**, particularly if the arthritis precedes onset of the skin disease

Spondylitis

the **impact of spondylitis on pain and function in PsA was similar in magnitude to ankylosing spondylitis** although it is **more likely to be unilateral in PsA**.

In addition, **gastrointestinal (GI) inflammation is less commonly** observed in psoriatic spondylitis compared to AS.

Measures used to assess AS (BASDAI, Shober score, chest expansion, occiput to wall distance and lateral flexion) **can be used in the evaluation and longitudinal monitoring of PsA patients** with spinal involvement.

Enthesitis

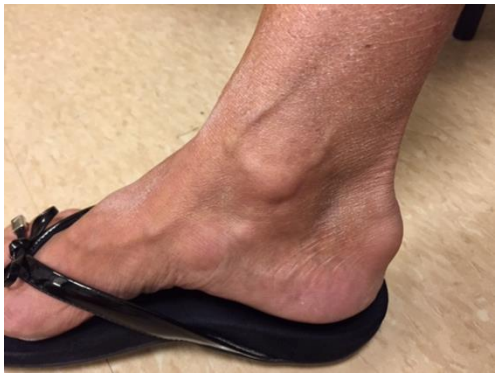
Enthesitis >>> (inflammation at insertion sites of tendons, ligaments, and joint capsules onto bone)

is a central element of the spondyloarthropathies.

- **Common sites of involvement include**
  - the plantar fasciae,
  - patellar and quadriceps tendons insertion
  - Achilles tendons,
  - insertion sites in the iliac crest and the rotator cuff.
- **Patients present with**
  - localized pain
  - occasionally swelling at the insertion or more widespread discomfort

it must be differentiated from fibromyalgia or other chronic pain syndromes.

Enthesitis



Subclinical enthesitis

(detected by ultrasound) is quite common in psoriasis patients although isolated enthesitis as a clinical feature is not common in PsA.

Examination of enthesial sites

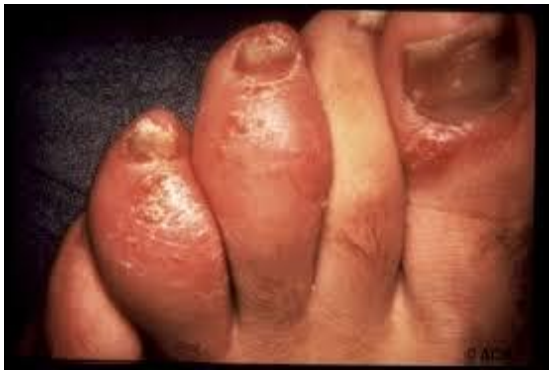
can be performed rapidly in the clinic and should be part of the musculoskeletal examination in all patients with psoriasis and possible psoriatic arthritis.

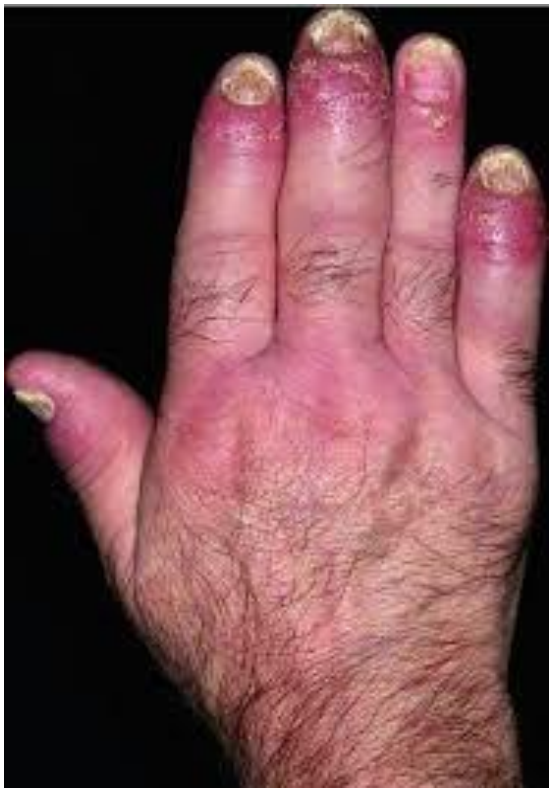
Dactylitis

Diffuse swelling of a ray or ‘sausage digit’ is considered a

characteristic finding in PsA,

- **it can also be observed in**
  - **Other forms of spondyloarthritis,**
  - **Sarcoidosis,**
  - **gout,**
  - **Sickle cell disease, and**
  - **Tendon sheath infections.**





Dactylitis

In PsA, inflammation can be **acute** (tender) or **chronic** (non-tender);

both forms have been **associated with joint erosions and new bone formation.**

Dactylitis is considered a **marker of severity** because it is associated with polyarticular disease and bone erosions.

Other findings associated with PsA

Uveitis

Up to **10% of patients** with PsA develop uveitis, which is seen most frequently in **males who are HLA-B27 positive**.

it is **more often bilateral, insidious in onset, can involve the posterior pole of the eye**, and often requires NSAIDs or additional immunosuppressive therapy.

axial disease, uveitis, and colitis cluster together in PsA patients, perhaps linked by an **HLA-B27-dependent mechanism**,

Metabolic syndromes and other comorbidities

Psoriasis and PsA patients also have a significantly higher rate of **obesity, insulin resistance, type 2 diabetes, and metabolic syndrome** than age-matched controls.

In addition, **hypertension, hyperlipidemia and cardiovascular disease, including myocardial infarction** are more common in patients with psoriasis and PsA than controls.

Aggressive risk-factor modification and suppression of inflammation might lessen the frequency and severity of these comorbidities.

Psoriasis mimics / D.D. of PsA

Psoriasis mimics / D.D. of PsA

Psoriasis Mimics

- **Eczema,**
- **Cutaneous T cell lymphoma,**
- **Seborrheic dermatitis,**
- **Tinea corporis and cruris,**
- **Discoid and subacute lupus and**
- **Lichen planus.**

A skin biopsy should be strongly considered, particularly in patients with **atypical clinical phenotypes**.

Differential Diagnosis

- **Rheumatoid arthritis,**
- **Reactive arthritis,**
- **Ankylosing spondylitis,**
- **Axial spondyloarthritis,**
- **Enteropathic arthritis,**
- **SLE,**
- **Osteoarthritis.**

Fibromyalgia can also mimic enthesitis and can co-occur with PsA.

What tests to perform?

Laboratory testing

The most important role of lab testing is to exclude other considerations in the differential diagnosis.

Anti-cyclic citrullinated peptide (anti-CCP) antibodies and antinuclear antibodies (ANA) may be helpful in some patients if there are symptoms that suggest a diagnosis of RA or systemic lupus erythematosus (SLE).

However, some patients with psoriatic arthritis alone may have positive tests.

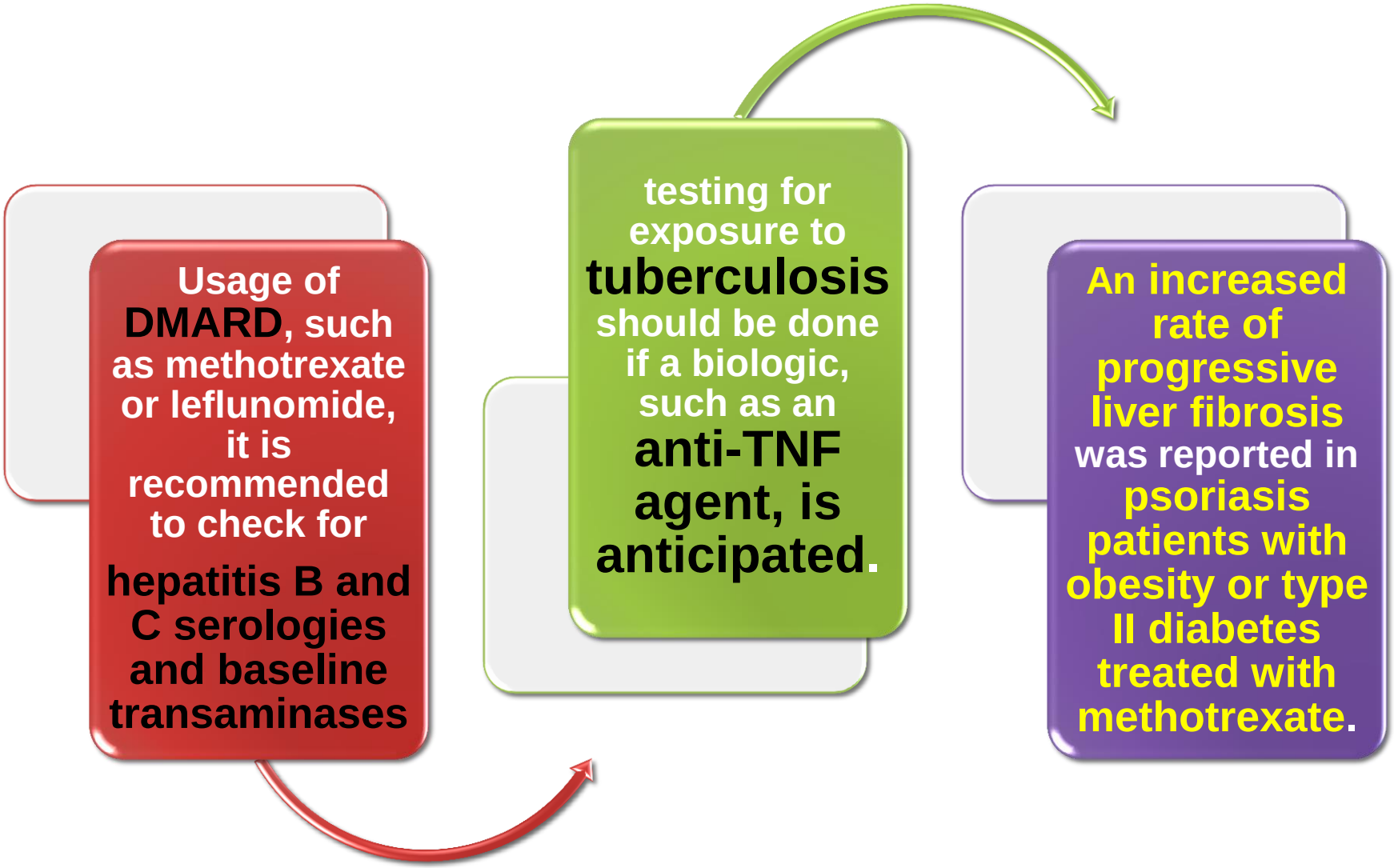
Acute phase reactants (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) may provide insights into disease activity,

although many patients with active PsA have normal acute phase reactants.

Metabolic and comorbidities lab

- lipid profile since obesity
- metabolic syndrome
- type 2 diabetes
- fatty liver
- hyperlipidemia
- It is also critical to ensure that women of child-bearing age are not pregnant so a pregnancy test may be required.

In patients who are under consideration for a DMARD




Imaging
studies

Imaging

The **heterogeneity of clinical** features in PsA can provide **unique challenges** to the clinician.

Fortunately, a number of imaging modalities can assist in **diagnosis**, **management, and assessment of treatment response**.

Imaging studies also play an increasing role in the **analysis of disease mechanisms** (enthesitis, dactylitis, new bone formation) as well.

Plain radiography

Early inflammatory changes in PsA affect **soft tissue and bone marrow** and **cannot be detected with the use of plain radiography**, or the image is indistinctive (for example soft tissue swelling, increased radiodensity of juxtaarticular soft tissue).

With the disease progression this image becomes **similar to RA, i.e. joint space narrowing and erosions develop**.

Characteristic radiographic features of PsA occur in an **advanced disease**

Peripheral joints

Typical inflammatory destructive lesions in hand and foot in PsA are as follows :

- **dactylitis** (so-called sausage digit) seen on radiographs as soft tissue swelling of an entire digit resulting from inflammatory changes in the DIP and PIP joints, flexor tenosynovitis, finger's joints synovitis or inflammation of subcutaneous and extrasynovial soft tissues;
- **marked deformity of fingers**;
  - destructive changes, i.e. subchondral cyst and erosions, are commonly detected in DIP joints of hand and foot and IP joint of the big toe with distinctive spike-like or fluffy proliferative alterations on joint surface margins and phalangeal tuft;
- **phalangeal tuft acroosteolysis;**
  - osteolytic lesions of the phalanx, which constitutes socalled pencil in cup deformity;
- **bone ankylosis;**
- **coexistence of osteolysis and ankylosis in joints of the same anatomical region** (hand, foot);
- **periostitis along metaphyses and shafts** of digits of the hand and foot;
- **perisoteal and endosteal bone formation**, which may increase bone density of an entire phalanx (*ivory phalanx*);
- **juxtaarticular and gross osteoporosis (less frequent than in RA);**
- **asymmetric distribution**.

Plain radiography

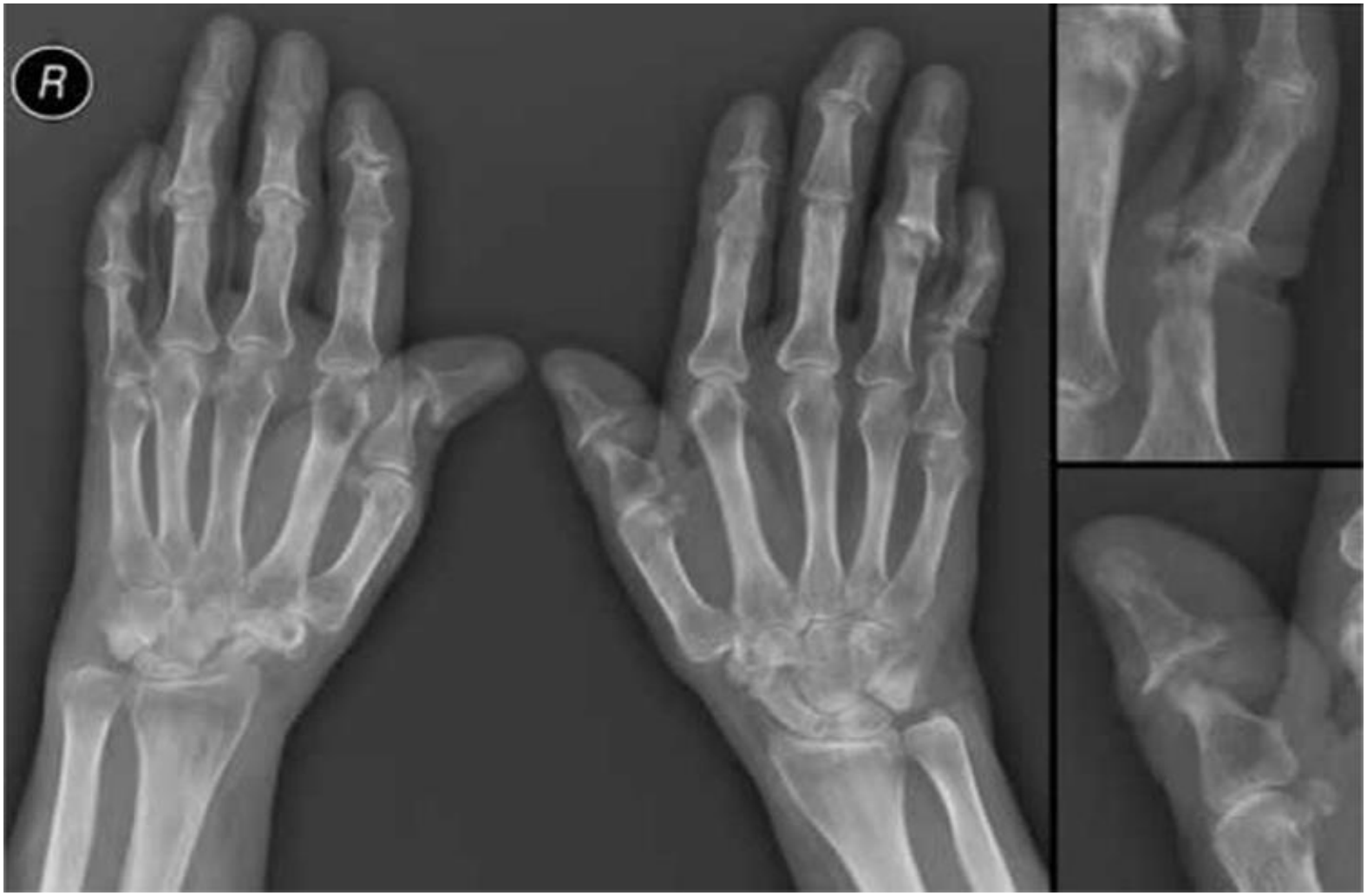
Out of 7 radiological features seen in hand and feet joints

- **interphalangeal bony ankylosis,**
- **DIP erosive changes,**
- **juxtaarticular new bone formation,**
- **joint osteolysis,**
- **radiographic involvement,**
- **tuft osteolysis,**
- **any peripheral X-ray feature**

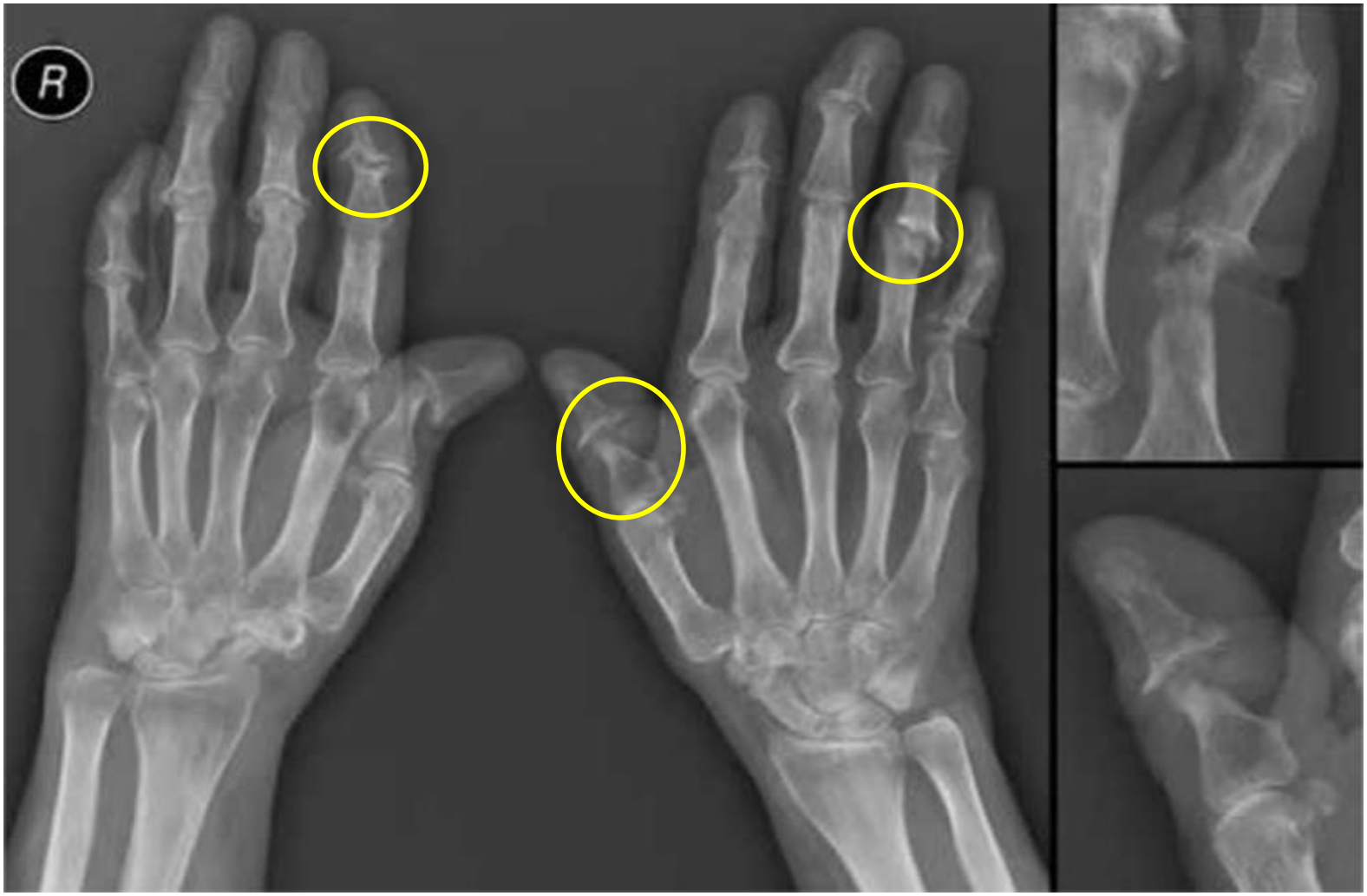
juxtaarticular new bone formation, joint osteolysis and phalangeal periostitis were excellent markers of PsA.

However, the only feature independently associated with PsA in a multivariate logistic regression analysis was juxtaarticular new bone formation. Thus, it was the one included in CASPAR criteria.

Plain radiographs



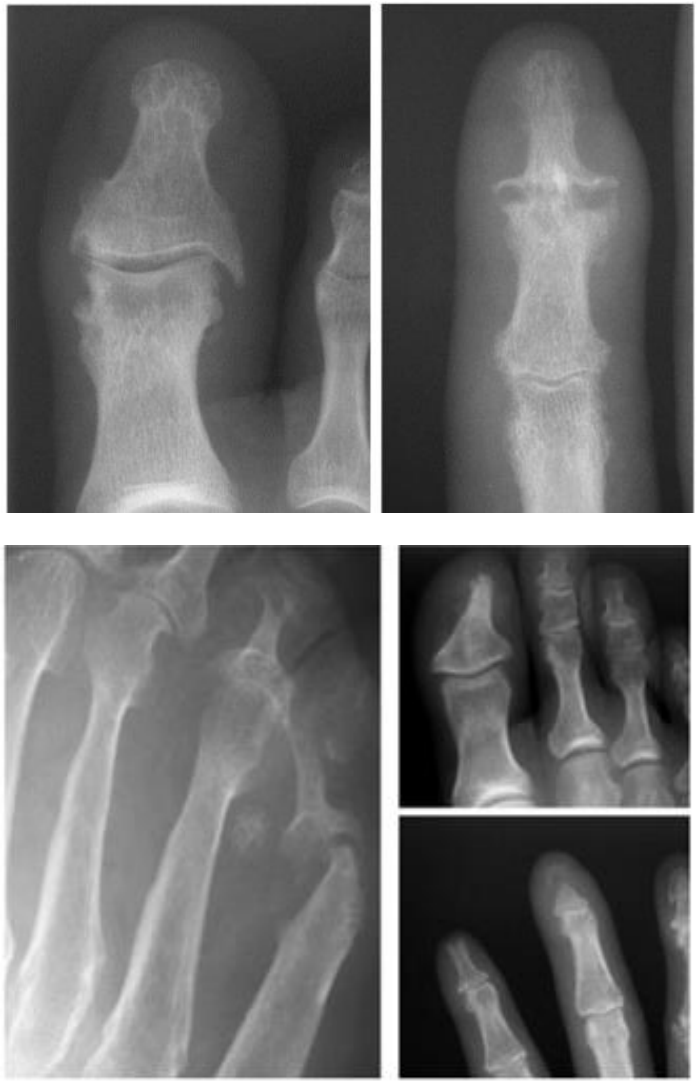
Plain radiographs

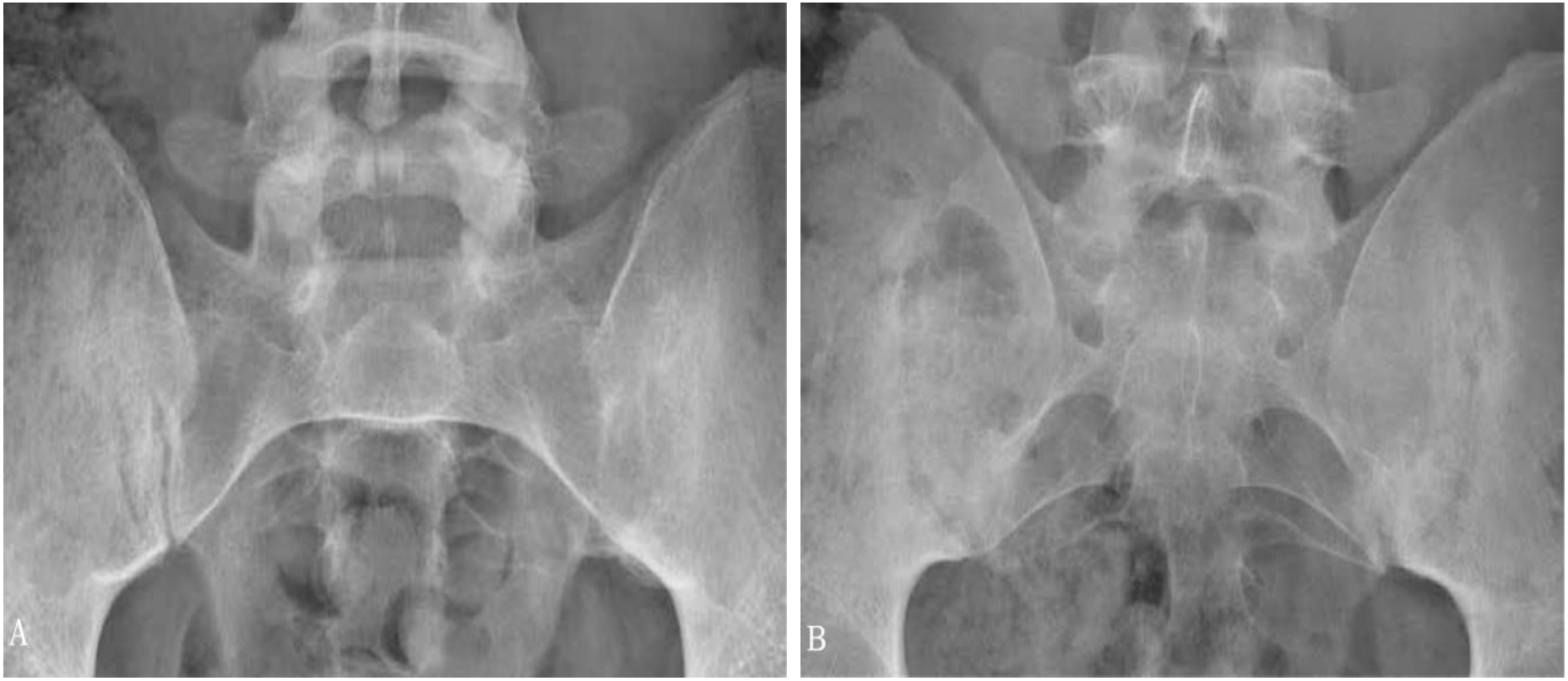


X-rays & PsA

Compared with RA:

- Asymmetric erosions
- Reduced osteopenia
- New bone formation
- Acro-osteolysis





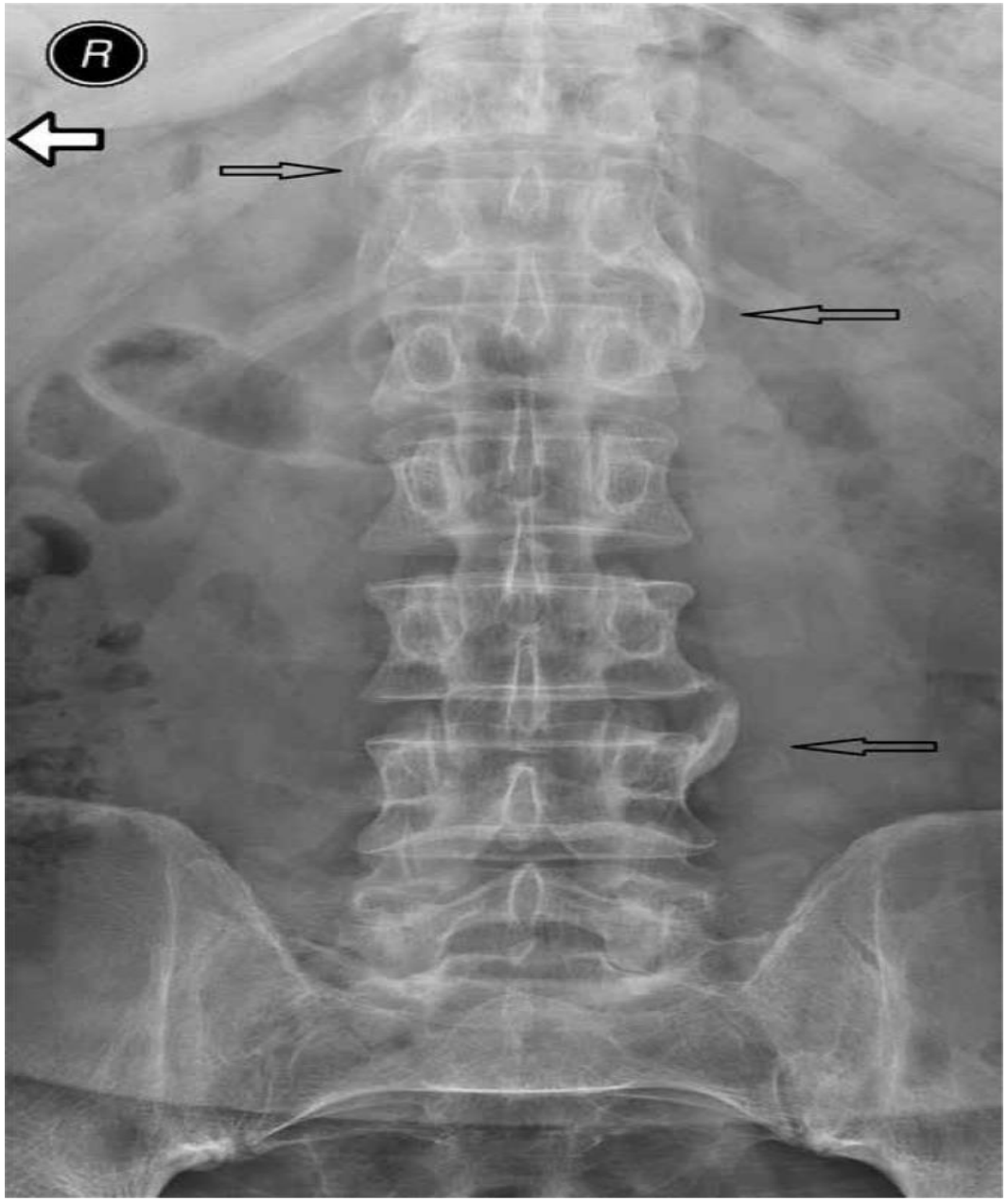
AP radiograph of the sacroiliac joints:
A. bilateral sacroiliitis, **grade 2 on the right, grade 4 on the left**,
B. ill-defined articular surface of the sacroiliac joints and subchondral bone osteosclerosis, partial and simultaneous widening and narrowing of the joint space (erosions and early ankylosis), image indicative of **bilateral sacroiliitis, grade** 3

Lumbar spine AP X-ray of the 34 y.o. female patient with suspected PsA:

osteoporosis,

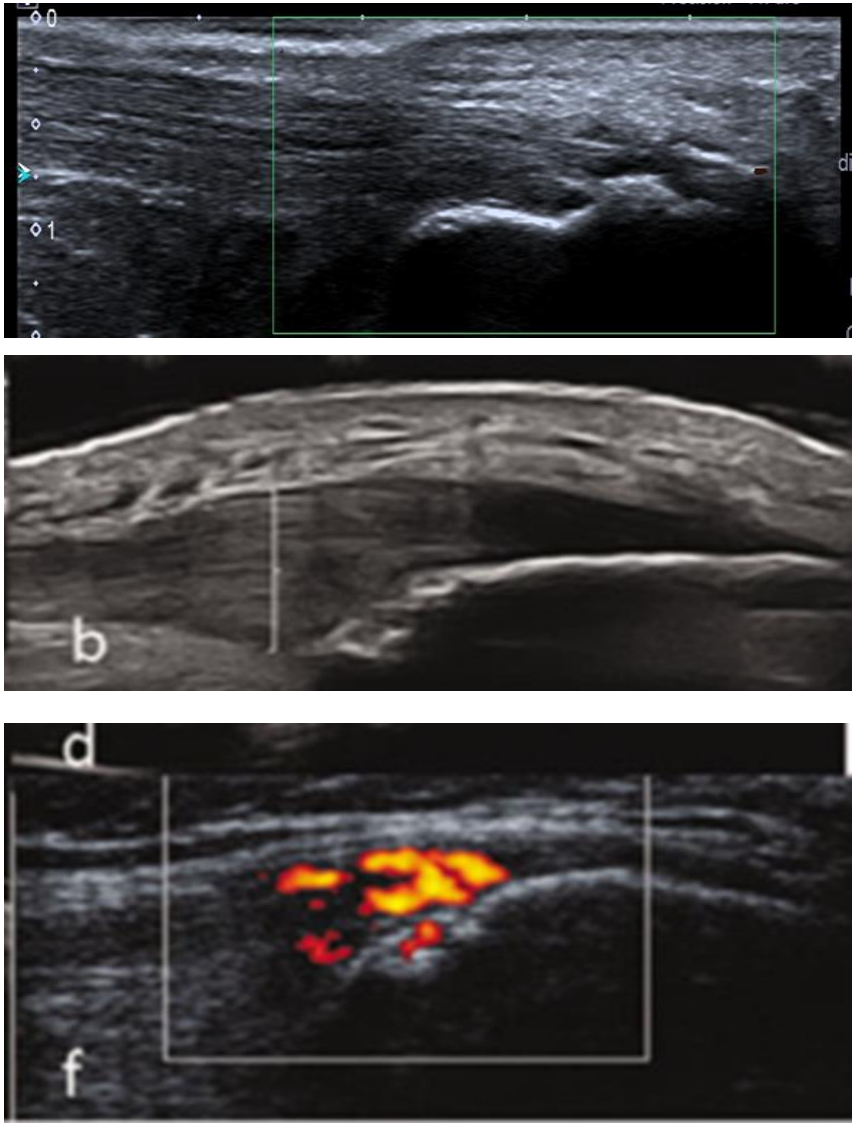
parasyndesmophytes in the thoracolumbar junction and on the left side of 4th lumbar vertebra (arrows),

uneven articular surface of the sacroiliac joints as in erosions – changes indicative of bilateral sacroiliitis, grade 2



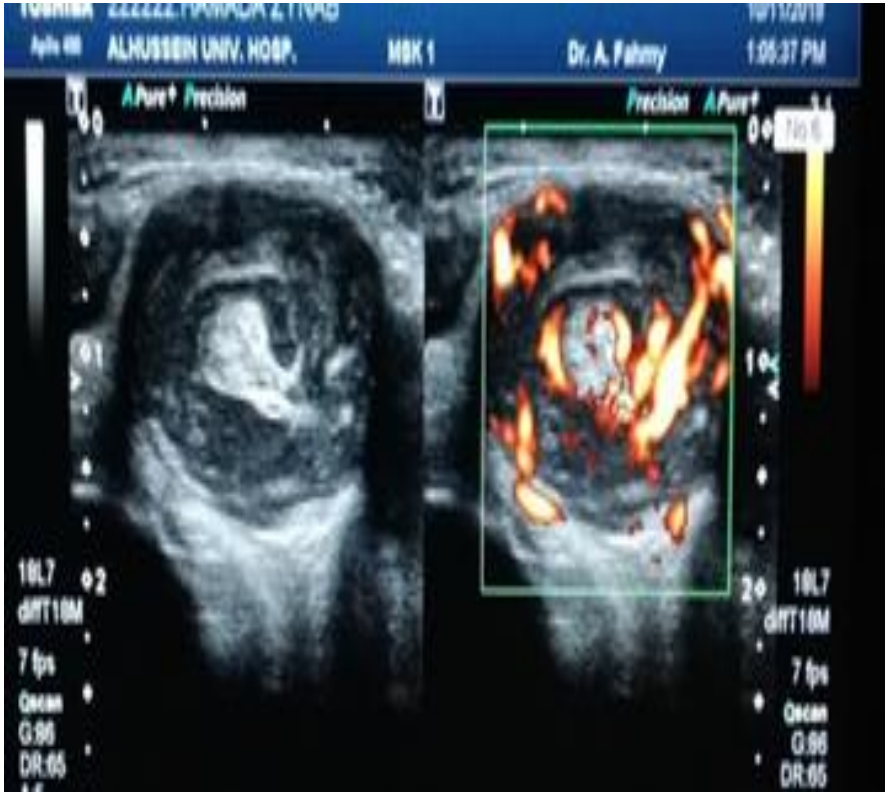
Musculoskeletal ultrasound

has rapidly emerged as an important imaging modality in PsA because it can visualize entheseal and synovial inflammation along with early erosions.



Synovitis and tenosynovitis

- **Ultrasound shows a typical spectrum of pathologies**, like in other inflammatory processes:
  - **exudate,**
  - **synovial pathology, i.e. thickening and**
  - **increased vascularisation, with**
  - **the following destructive component.**
- As far as sausage digit (dactylitis) is considered, **US can differentiate subcutaneous edema with tenosynovitis and synovitis**.
- Extra-synovial soft tissue inflammation in 84% of cases (pseudosynovitis), including 60% coexisting with synovitis of the finger joints.
- **Comparing ultrasonographic features of PsA and RA** :
  - **enthesitis, subcutaneous soft tissue thickening and a positive Doppler signal at the base of the nail are suggestive of periungual psoriatic involvement, and may be indicative of PsA.**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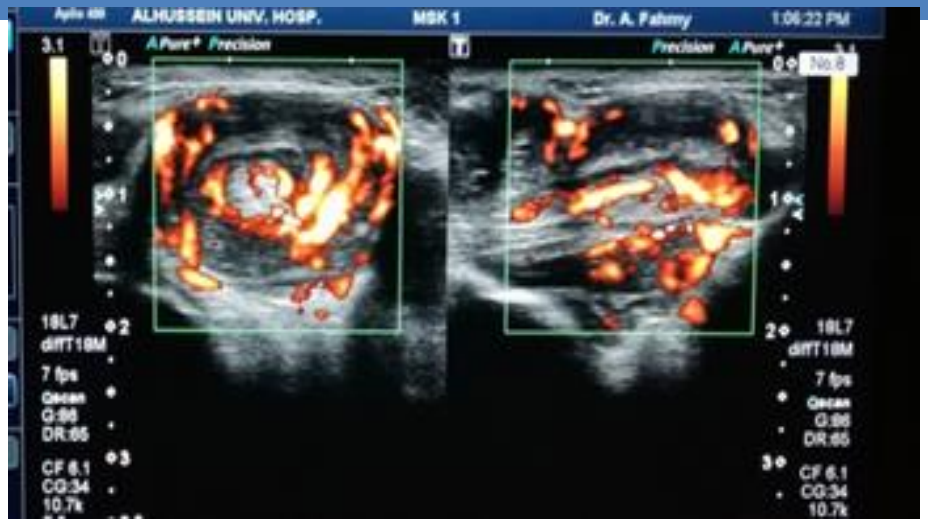
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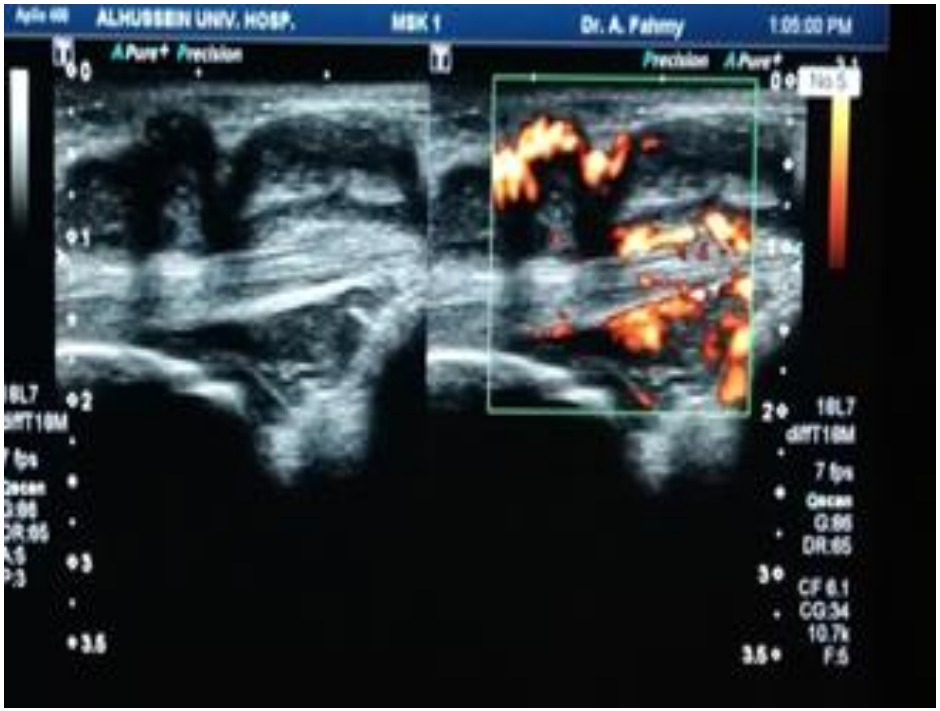
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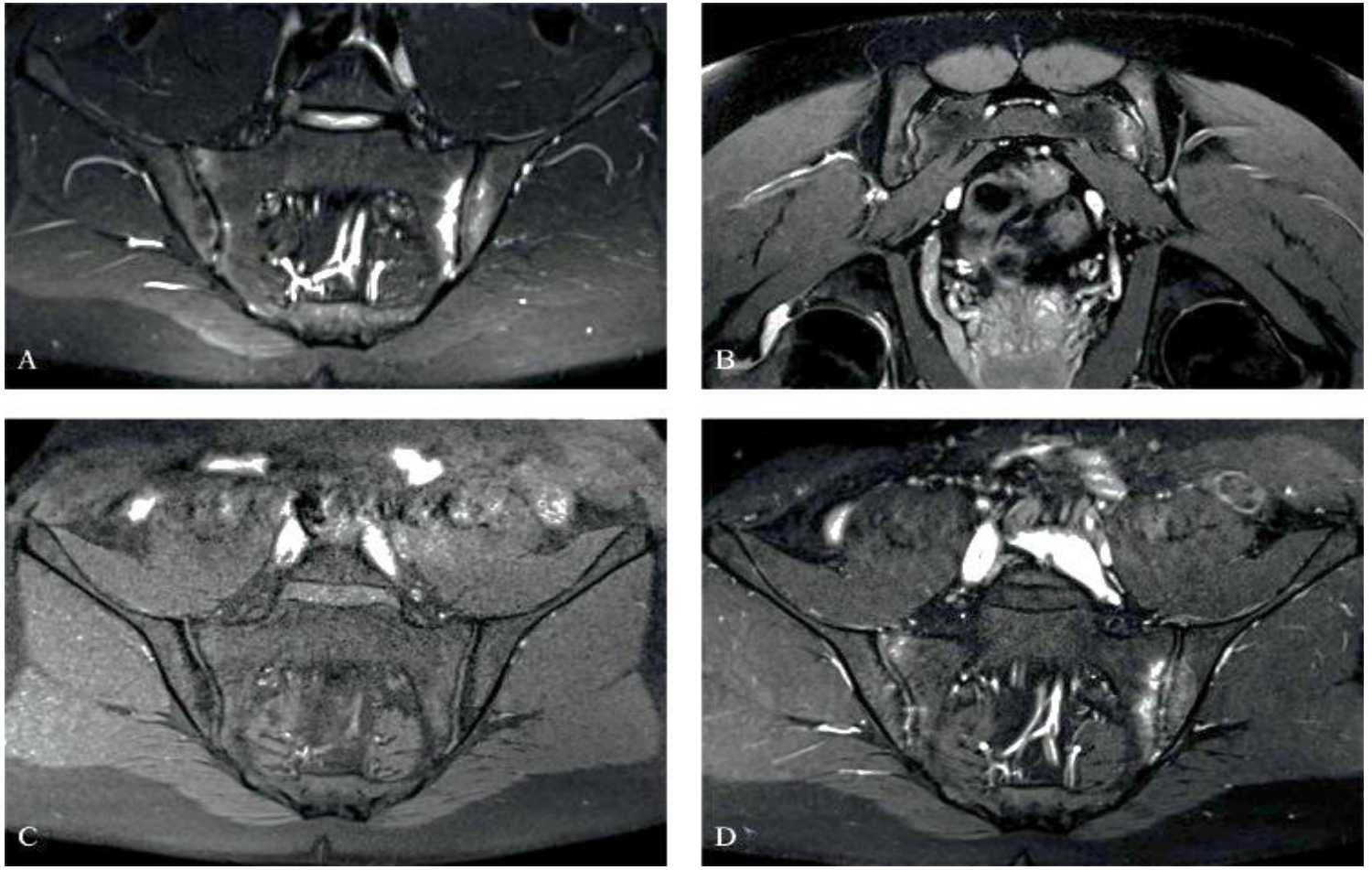
MRI

- reveal bone marrow edema, an important finding in PsA along with entheseal and synovial inflammation, and can also detect erosions.
- It must be emphasized, however, that many psoriasis patients have subclinical findings on imaging studies, although the significance of these abnormalities is not well understood.

Axial disease

With the introduction of ASAS (Assessment of SpondyloArthritis International Society) criteria, the use of MRI in detecting BME in the sacroiliac joints and the spine, in patients with all clinical forms of SpA, has become more common .

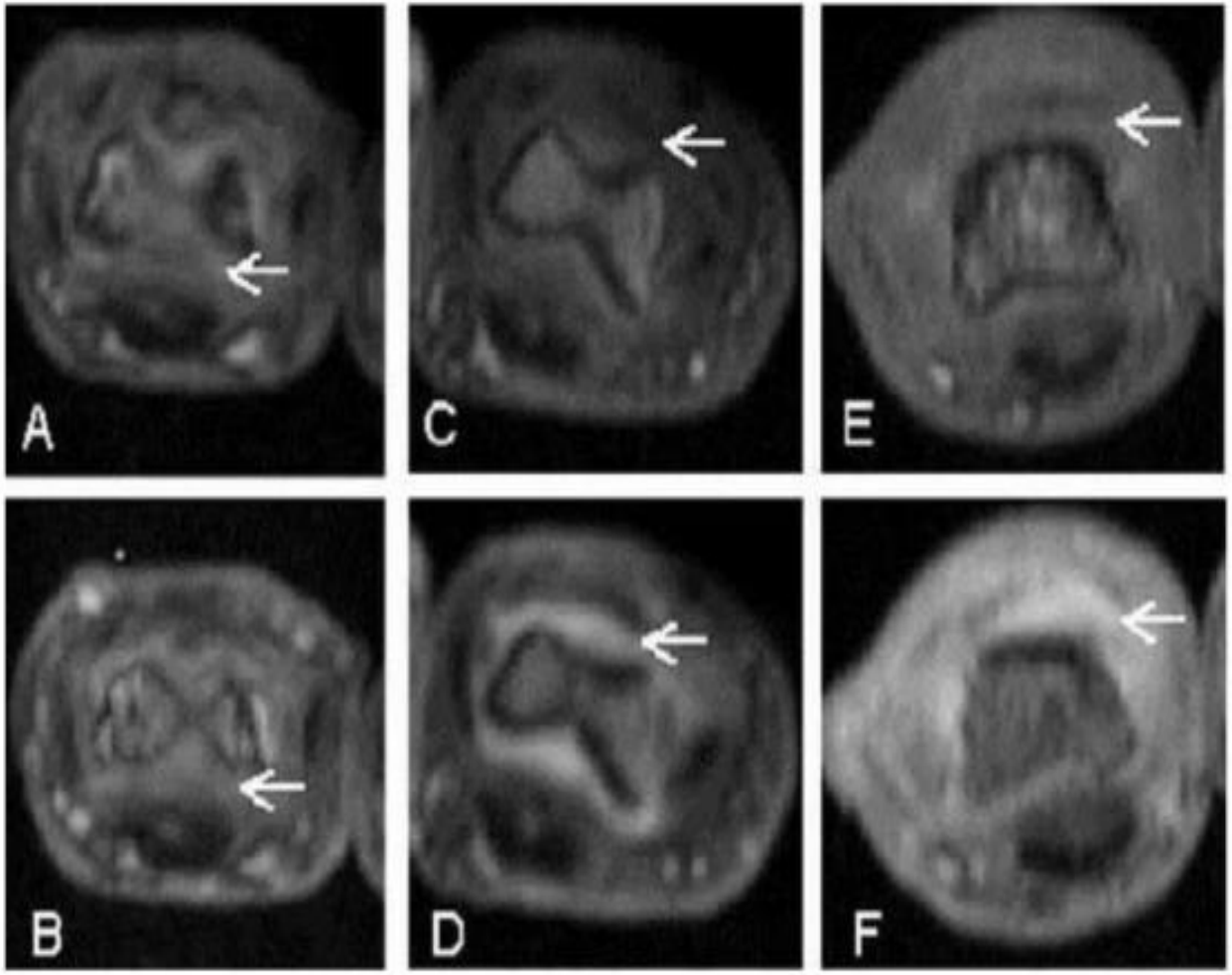
Namely, **HLA-B27 negative PsA patients had lower BME scores than HLA-B27 positive**



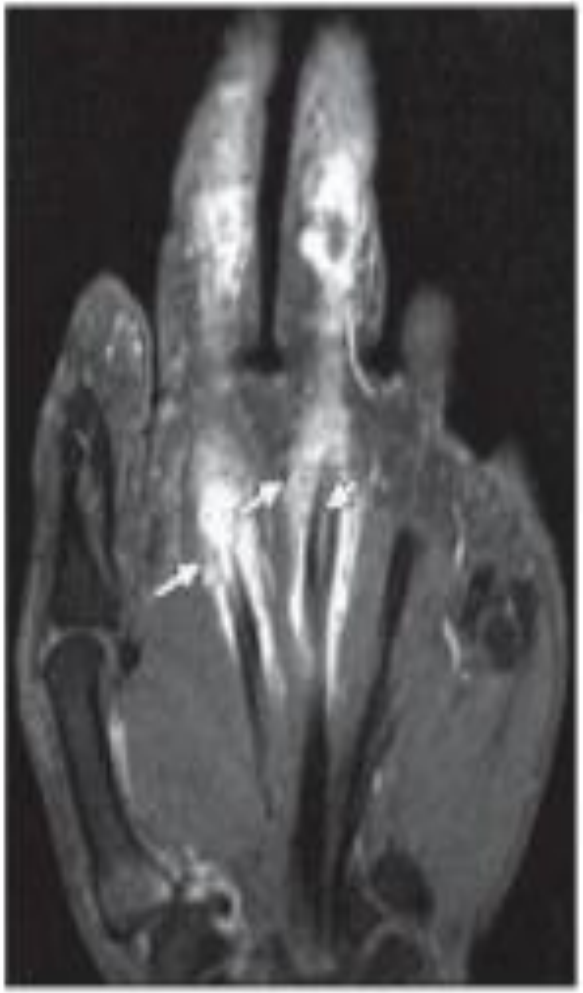
MRI of the sacroiliac joints in a 25 y.o. female with suspicion of PsA: ***A***. TIRM T2; ***B***. PD; ***C***. T1 FS; ***D***. T1 FS CM: bilateral subchondral bone marrow edema in the sacroiliac joints, with signal enhancement after contrast media administration, to the greater extent on the left side, bilateral minor bony erosions – bilateral sacroiliitis

MRI & PsA: Synovitis

- Pre-contrast
- Post-contras

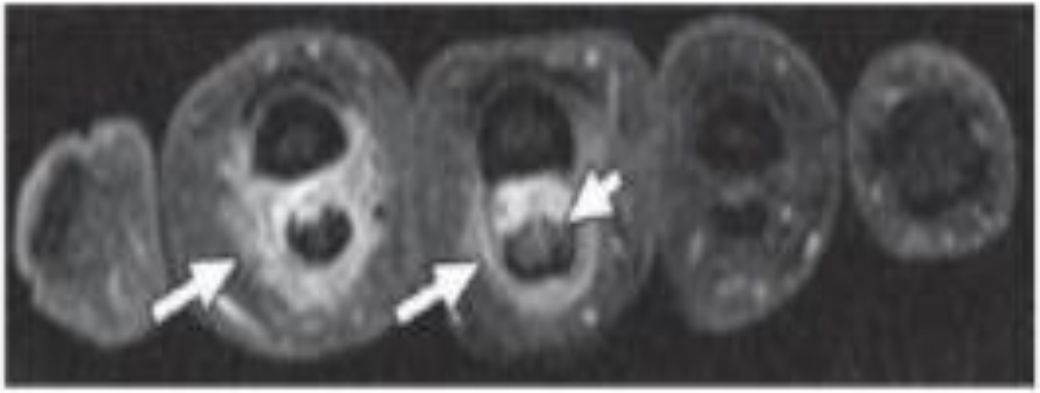


Tenosynovitis



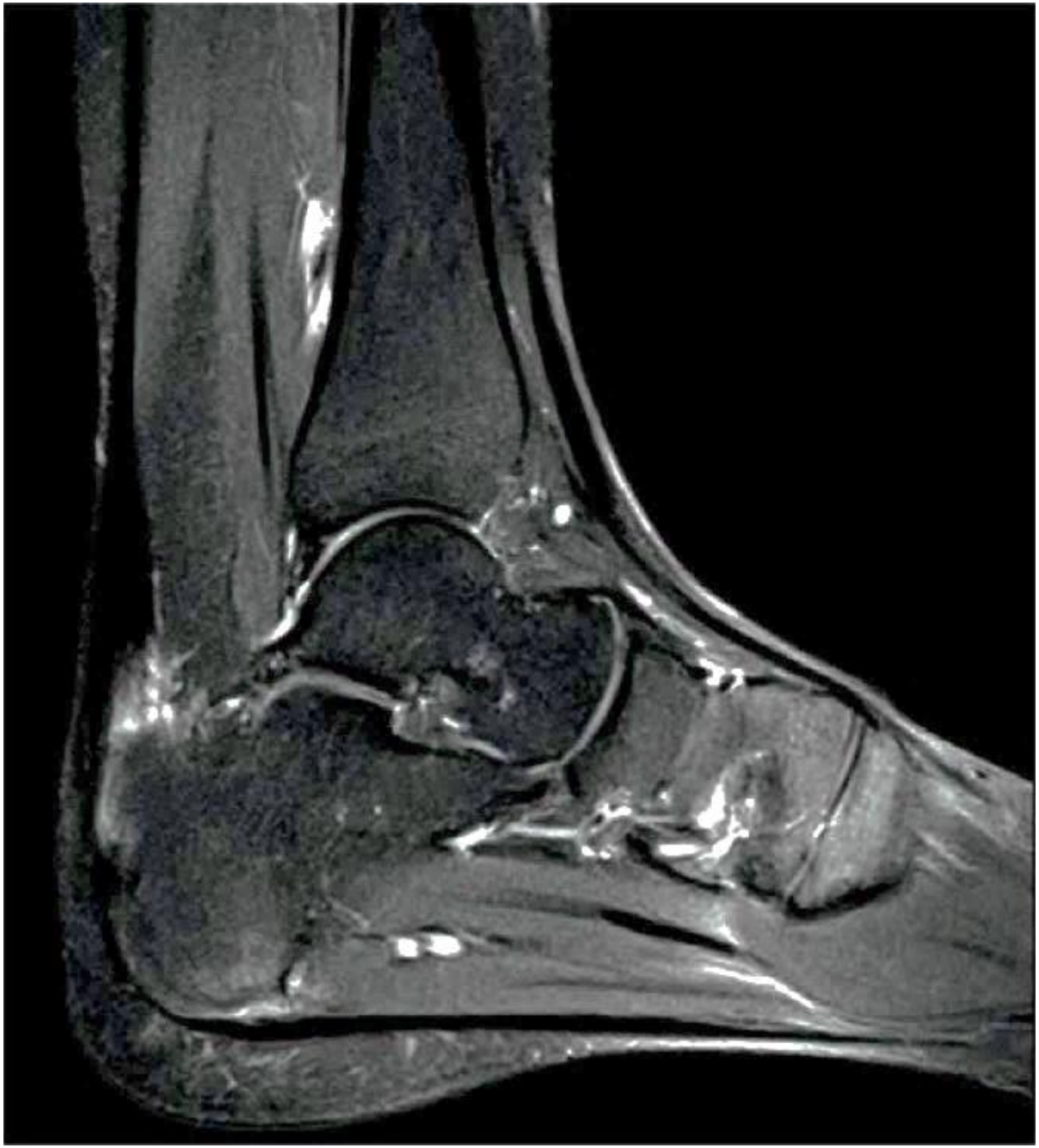
MRI, magnetic resonance imaging; PsA, psoriatic arthritis.

- Gadolinium-enhanced T1-weighted fat-saturated MRI of right hand show marked synovial and extrasynovial enhancement of flexor tendon sheaths of second and third digits (large arrows) and enhancement of corresponding tendons (small arrow



BME and bone erosions

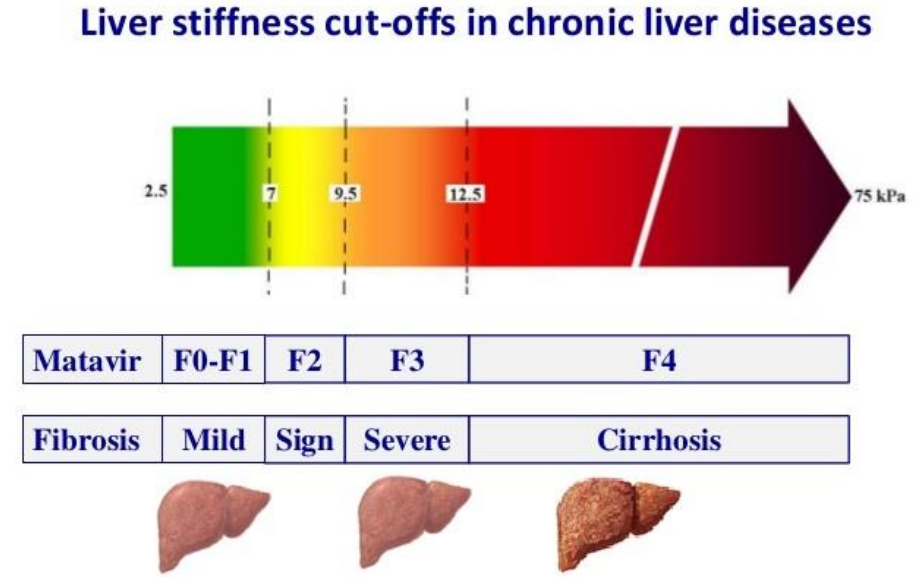
RA	PsA
Bone marrow edema in RA involves **typically subchondral layer of the bone**.	In PsA it is reported to be more extensive and **expanding to diaphysis**.
NO any differences in synovitis between RA and PsA.	**Enthesitis**, extensive BME in the bones' diaphyses and subcutaneous tissue involvement were specific for PsA.
However, as for tenosynovitis, **tendon sheaths of the extensors in RA**	as for tenosynovitis, tendon sheaths of the **flexors were more often involved in PsA**,
As far as bone erosions are considered, there is no MR detectable disparities between PsA and RA	BME is more severe in patients with arthritis mutilans PsA phenotype than in other clinical manifestations of this entity.



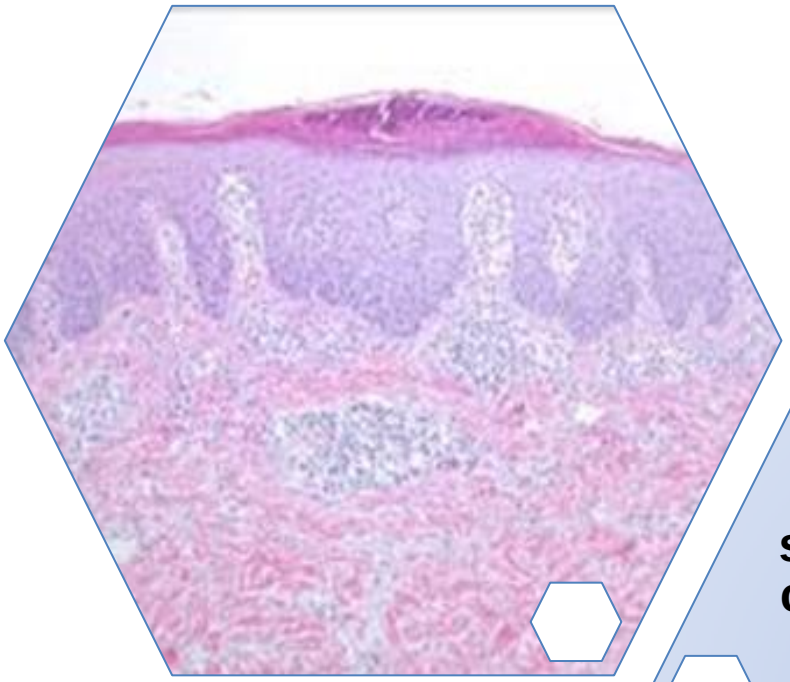
T1 FS sagittal plane MRI of the Achilles tendon in a 19 y.o. female with PsA: increased signal of the soft tissues adjacent to the plantar aponeurosis with bone marrow edema of the neighbouring part of the tuber calcanei, achillobursitis calcanei

fibroscan

- Fatty liver is commonly observed in patients with an elevated BMI and a fibroscan may be considered to evaluate for fibrosis and cirrhosis in patients with persistently elevated liver function tests.



Skin biopsy



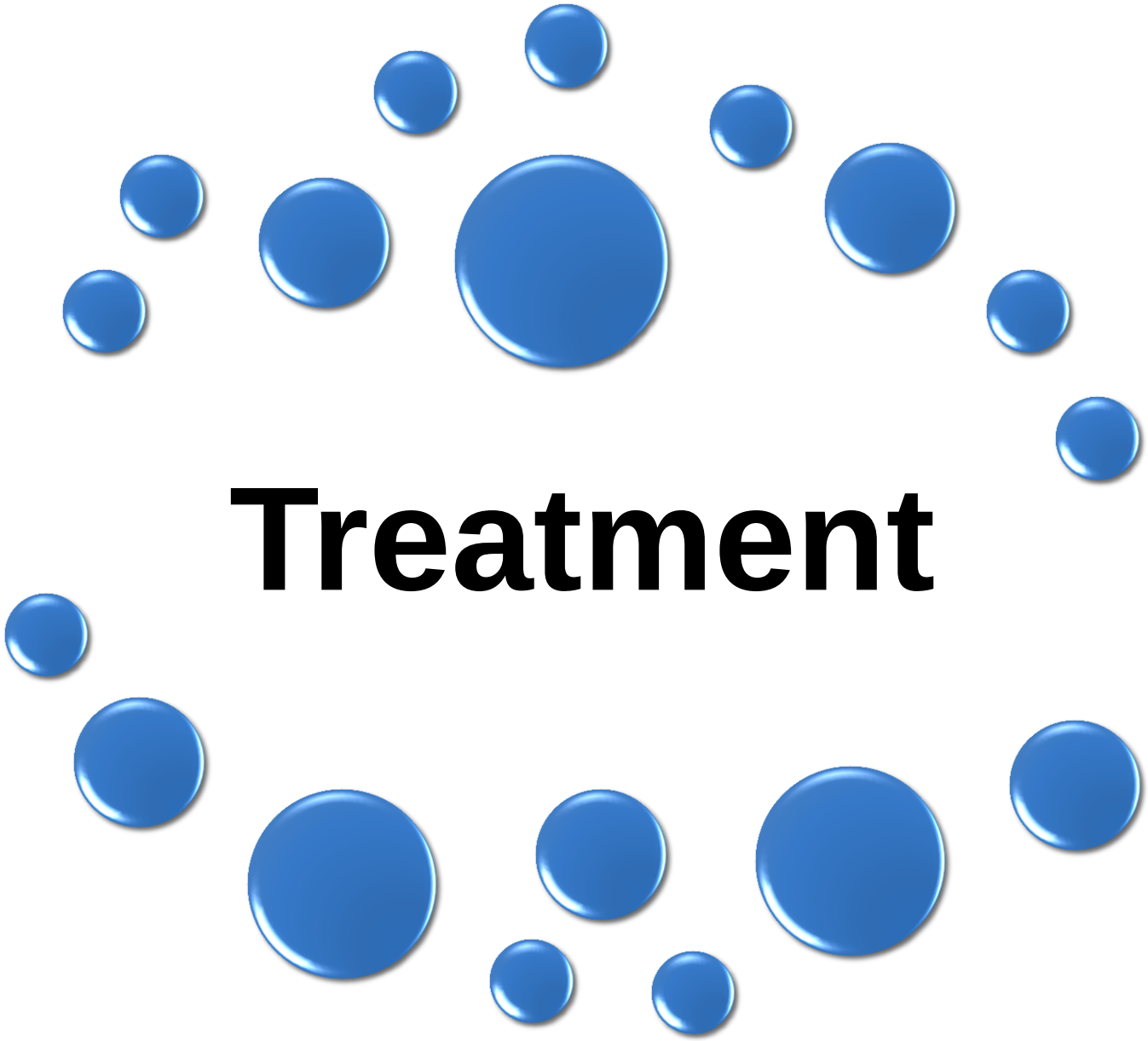
Skin biopsy is sometimes required to confirm a diagnosis of psoriasis to differentiate from eczema, subacute cutaneous lupus, cutaneous lymphoma, or syphilis.

Controversies in diagnostic testing

Occasionally, patients with **PsA will have a positive rheumatoid factor and/or anti-CCP antibody**.

The main differential diagnosis in this setting is psoriasis with RA or PsA with a serologic antibody that is not clinically significant.

Generally, **a careful physical exam** and **careful review of the X-rays and sometimes ultrasound or MRI** will help the clinician decide between these two possibilities



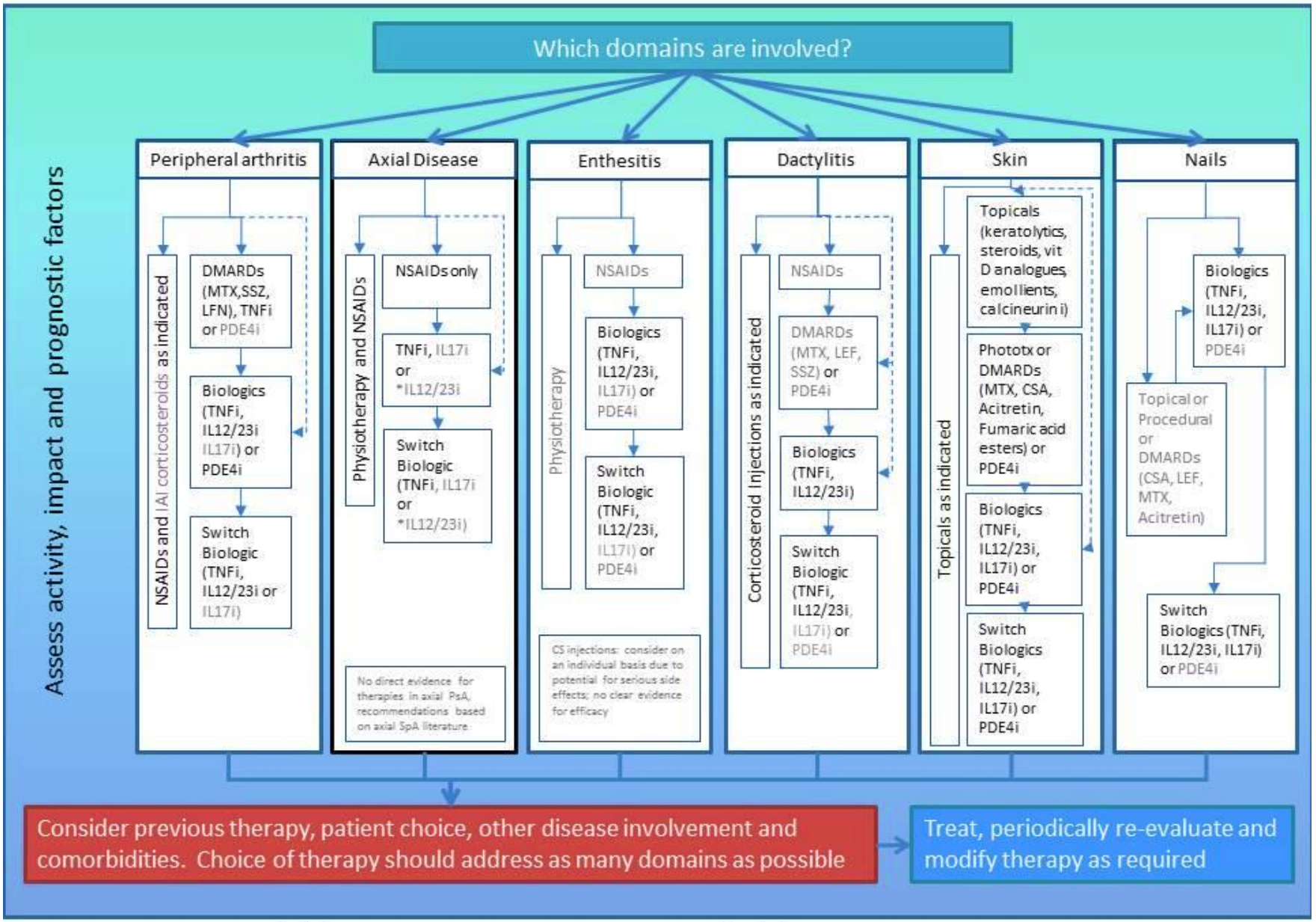
Treatment

How should patients with psoriatic arthritis be managed?

The articular and dermatologic manifestations associated with PsA are **remarkably heterogeneous in both the extent and type of tissue involvement.**

Heterogeneity is observed not only in disease manifestations **but also in severity and course**, which can vary from very mild psoriasis or enthesitis to widespread psoriatic plaques, disfiguring nail disease, and severe joint inflammation with destruction that can result in disability and increased mortality.

Moreover, **comorbidities associated** with psoriasis, such as the metabolic syndrome, can contribute to damage in multiple end-organs and often leads to markedly impaired QOL as well as early mortality.


Assess activity, impact and prognostic factors
Which domains are involved?
Peripheral arthritis
NSAIDs and IAI corticosteroids as indicated
DMARDs (MTX,SSZ, LFN), TNFi or PDE4i
Biologics (TNFi, IL12/23i IL17i) or PDE4i
Switch Biologic (TNFi, IL12/23i or IL17i)
Axial Disease
Physiotherapy and NSAIDs
NSAIDs only
TNFi, IL17i or *IL12/23i
Switch Biologic (TNFi, IL17i or *IL12/23i)
No direct evidence for therapies in axial PsA, recommendations based on axial SpA literature
Enthesitis
Physiotherapy
NSAIDs
Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Switch Biologic (TNFi, IL12/23i, IL17i) or PDE4i
CS injections: consider on an individual basis due to potential for serious side effects; no clear evidence for efficacy
Dactylitis
Corticosteroid Injections as indicated
NSAIDs
DMARDs (MTX, LEF, SSZ) or PDE4i
Biologics (TNFi, IL12/23i)
Switch Biologic (TNFi, IL12/23i, IL17i) or PDE4i
Skin
Topicals as indicated
Topicals (keratolytics, steroids, vit D analogues, emollients, calcineurin i)
Phototx or DMARDs (MTX, CSA, Acitretin, Fumaric acid esters) or PDE4i
Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Switch Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Nails
Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Topical or Procedural or DMARDs (CSA, LEF, MTX, Acitretin)
Switch Biologics (TNFi, IL12/23i, IL17i) or PDE4i
Consider previous therapy, patient choice, other disease involvement and comorbidities. Choice of therapy should address as many domains as possible
Treat, periodically re-evaluate and modify therapy as required
KEY
Standard Therapeutic Route
Expedited Therapeutic Route

New onset of psoriatic arthritis

For a patient with new onset of psoriatic arthritis, a key branch point in the decision process **is the presence or absence of erosions or joint space narrowing.**

If joint damage is present, it is common practice to start an anti-TNF agent .

If not, apremilast, methotrexate or leflunomide is an option,

it is very important to **avoid use** of this agents in patients who are **obese and have type II diabetes or steatosis** because of the risk of progressive liver disease.

Likewise, it should be **avoided** in patients who **consume alcohol on a regular basis**.

Leflunomide can also be effective for arthritis but it is not effective for psoriasis.

New onset of psoriatic arthritis

If a **patient without erosions does not respond** to apremilast, methotrexate or leflunomide,

it is common practice to **add an anti-TNF agent, and, frequently, methotrexate (MTX) is discontinued** if a patient responds to the anti-TNF drug, except in the case of **infliximab** where a low dose of MTX (7.5 mg per week) may lessen the development of drug-neutralizing antibodies.

It is common practice to switch to a second, or even a third, anti-TNF agent for primary or secondary non-responders to a first anti-TNF molecule.

It is not established if agents that block IL-12/23, IL-17 or Jak-STAT should be considered for early treatment of PsA since we do not have head-to-head data at this time.

For patients who cannot take or are non-responders to anti-TNF agents, apremilast, ustekinumab, or secukinumab are effective alternatives approved for treatment of PsA.

Anti-TNF agents

The anti-TNF agents (adalimumab, certolizumab, etanercept, golimumab, and infliximab) have shown efficacy for symptoms and signs of psoriasis and arthritis, and **they inhibit X-ray progression in this disease**.

Most importantly, they are **effective for all domains of disease** including psoriasis, peripheral arthritis, axial disease, dactylitis and enthesitis.

They are reasonably **well tolerated**, although the **high cost remains a major barrier for many patients**.

Paradoxically, some patients **develop psoriasis, alupus like reaction, uveitis, sarcoidosis or Crohn's disease** on anti-TNF agents.

Sometimes a **switch to another anti-TNF agent** is associated with resolution of the adverse event but in some patients **switch to a therapy in a different class is required.**

Ustekinumab &Secukinumab

- **Ustekinumab**, the anti-P40 antibody that binds to IL-12 and IL-23, was approved for PsA and is now an option for patients who cannot tolerate or do not respond to anti-TNF agents.
- Ustekinumab is also effective for enthesitis and dactylitis, and does slow radiographic progression.
- A phase III trial of **ustekinumab in ankylosing spondylitis was discontinued for lack of efficacy** so this agent may not be ideal for patients with psoriatic spondylitis.
- **Secukinumab** is also **approved for psoriasis and psoriatic arthritis**.
- This agent is an **IL-17A antagonist** that is **effective for dactylitis and enthesitis and also inhibits radiographic progression**.
- Secukinumab is also approved for ankylosing spondylitis and provides another option for patients with **axial manifestations of PsA**.

Pharmacologic considerations

Patients with psoriasis and PsA are frequently **on multiple medications**.

They are often taking **topical agents** for psoriasis and either **oral meds or injectable agents** for psoriasis and PsA.

Add to this the **high prevalence of comorbidities** (**metabolic syndrome, cardiovascular disease, obesity**) and the list of medications can become formidable.

Thus, it is essential to **simplify the treatment regimen** as much as possible **to maintain compliance**.

Obesity has also been associated with a reduced response to anti-TNF

patients with **obesity** and severe psoriasis and/or psoriatic arthritis **may respond better to a drug that is administered using a weight based regimen** (infliximab) or that targets other molecules

How to utilize team care?

Specialty consultations include

- dermatology,
- orthopedics,
- podiatry,
- endocrinology,
- cardiology.

Dermatology nurses with expertise in wound care.

Dieticians are key members of the team because of the high prevalence of obesity and metabolic syndrome.

Physical and occupational therapists and pedorthists are integral members of the team

Take Aways for PsA

- **Early diagnosis** and early, aggressive treatment should aim to halt or minimize joint damage and clearing skin psoriasis
- **Treat key clinical domains** (i.e., arthritis, spondylitis, enthesitis, dactylitis, skin, and nail disease)
- Be aware of **comorbidities** and their implication to treatment approaches
- **Collaborate** with an interdisciplinary approach to screening and managing patients
- **Apply treat-to-target strategies** to improve patient outcomes
- **Educate patients** on range of available treatments and new options
- **Help patients gain a better understanding** of their condition and how to manage it


THANK
YOU!